Amendment to the Specification

Please replace paragraph [0004] with the following amended paragraph:

[0004] Various nicotinic compounds have been reported as being useful for treating a wide variety of conditions and disorders. See, for example, Williams et al., Drug News Perspec. 7(4):205 (1994); Arneric et al., CNS Drug Rev. ~~1(1):~~ 1(1)1: (1995); Arneric et al., Exp. Opin. Invest. Drugs 5(1):79 (1996); Bencherif et al., J. Pharmacol. Exp. Ther. 279:1413 (1996); Lippiello et al., J. Pharmacol. Exp. Ther. 279:1422 (1996); Damaj et al., J. Pharmacol. Exp. Ther. 291:390 (1999); Chiari et al., Anesthesiology 91:1447 (1999); Lavand'homme and Eisenbach, Anesthesiology 91:1455 (1999); Holladay et al., J. Med Chem. 40(28): 4169 (1997); Bannon et al., Science 279: 77 (1998); PCT WO 94/08992, PCT WO 96/31475, PCT WO 96/40682, and U.S. Pat. Nos. 5,583,140 to Bencherif et al., 5,597,919 to Dull et al., 5,604,231 to Smith et al. and 5,852,041 to Cosford et al. Nicotinic compounds are reported as being particularly useful for treating a wide variety of CNS disorders. Indeed, a wide variety of compounds have been reported to have therapeutic properties. See, for example, U.S. Pat. Nos. 5,1871,166 to Kikuchi et al., 5,672,601 to Cignarella, PCT WO 99/21834 and PCT WO 97/40049, UK Patent Application GB 2295387 and European Patent Application 297,858.

Please replace paragraph [0073] with the following amended paragraph:

[0073] ~~3-(5-phenyl-3-pyridyl)-3,7-diazabicyclo[3.3.2]nonane~~ 3-(5-phenyl-3-pyridyl)-3,7-diazabicyclo[3.3.1]nonane

Please replace paragraph [0093] with the following amended paragraph:

[0093] The 3,6-diazabicyclo[3.2.2]nonane ring system can also be coupled to aryl halides via the 6-aza position, producing 6-aryl-3,6-diazabicyclo- [3.2.2]nonanes, which are isomeric to the 3-aryl-3,6-diazabicyclo[3.2.2]no- nanes described previously. Thus, the aforementioned 3-benzyl-6-carboethoxy-3,6-diazabicyclo[3.2.2]nonane can be hydrolyzed to 3-benzyl-3,6-diazabicyclo[3.2.2]nonane, which can subsequently be coupled to an aryl halide in a palladium-catalyzed reaction. The 6-aryl-3-benzyl-3,6-diazabicyclo[3.2.2]nonane product can then be hydrogenated to give a ~~6-aryl-3,6-diazabicyclo[3.2.2]nonane~~ 6-aryl-3,6-diazabicyclo[3.2.2]nonane.

Please replace paragraph [0112] with the following amended paragraph:

[0112] Binding of the compounds to relevant receptor sites was determined in accordance with the techniques described in U.S. Pat. No. 5,597,919 to Dull et al. Inhibition constants (~~K~~, K_i values), reported in nM, were calculated from the IC_{50} values using the method of Cheng et al., Biochem. Pharmacol. 22:3099 (1973). ~~el~~

Example 1

Please replace paragraph [0117] with the following amended paragraph:

[0117] In a sealed pressure tube under an argon atmosphere, 3-bromo-5-(4-methoxyphenoxy)pyridine (0.37 g of 94%, 1.2 mmol), (1S,4S)-N-(tert-butoxycarbonyl)-2,5-diazabicyclo[2.2.1]heptane (0.21 g, 1.1 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.02 g, 0.02 mmol, ~~rac-2,2□-bis(diphenylphosphino)-1,1□-binaphthyl~~ rac-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.025 g, 0.04 mmol), sodium tert-butoxide (0.20 g, 2.0 mmol) and toluene (12 mL) were stirred at 80°C for 24 h. The reaction mixture was poured into saturated aqueous sodium chloride solution (20 mL) and extracted with diethyl ether (3 X 30 mL). The combined diethyl ether extracts were washed with saturated aqueous sodium chloride solution (20 mL), dried (Na_2SO_4), filtered and concentrated to a brown oil (0.37 g). The material was used without further purification.

Please replace paragraph [0128] with the following amended paragraph:

[0128] (1S,4S)-2-(5-(3-Methoxyphenoxy)-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane

To a stirred solution of (1S,4S)-5-(5-(3-methoxyphenoxy)-3-pyridyl)-2-(tert-butoxycarbonyl)-2,5-diazabicyclo[2.2.1]heptane (0.62 g, 1.5 mmol) in anisole (3.5 mL) at 0-5°C and under a nitrogen atmosphere, trifluoroacetic acid (2.5 mL) was added drop-wise over a 10 min period. After 0.5 h at 25°C, the solution was adjusted to pH 5 using 10% NaOH, followed by extraction with diethyl ether (1 X 15 mL) to remove the anisole. The aqueous portion was adjusted to pH 11 using 10% NaOH, followed by extraction with diethyl ether (3 X 25 mL). The combined diethyl ether extracts were dried (Na_2SO_4), filtered, and concentrated under vacuum to give a colorless oil (0.41 g, 82%).

Please replace paragraph [0136] with the following amended paragraph:

[0136] In a sealed pressure tube under a nitrogen atmosphere, 3-bromo-5-(4-fluorophenoxy)pyridine (1.4 g, 5.2 mmol), (1S,4S)-N-(tert-butoxycarbonyl)-2,5-diazabicyclo[2.2.1]heptane (1.24 g, 6.2 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.1 g, 0.1 mmol), ~~rac-2,2□-bis(diphenylphosphino)-1,1□-binaphthyl~~ rac-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.125 g, 0.2 mmol), sodium tert-butoxide (1 g, 10 mmol) and anhydrous toluene (50 mL) were stirred at 90°C for 20 h. The reaction mixture was cooled to room temperature and diluted with water (150 mL) and then extracted with diethyl ether (2 X 100 mL). The combined diethyl ether extracts were dried ($MgSO_4$), filtered and concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel, using a gradient of 33% to 67% ethyl acetate:hexane as eluent, to yield 1.8 g (90%) of a yellow oil.

Please replace paragraph [0144] with the following amended paragraph:

[0144] In a sealed pressure tube under an argon atmosphere, 5-(3-thienyl)-3-bromopyridine (0.37 g, 1.5 mmol), (1S,4S)-N-(tert-butoxycarbonyl)-2,5-diazabicyclo[2.2.1]heptane (0.31 g, 1.5 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.030 g, 0.033 mmol), ~~rac-2,2□-bis(diphenylphosphino)-1,1□-binaphthyl~~ rac-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.0375 g, 0.059 mmol), sodium tert-butoxide (0.30 g, 3.0 mmol) and toluene (15 mL) were stirred at 80°C for 24 h. The reaction mixture was dissolved in water (15 mL) and then extracted with diethyl ether (3 X 30 mL). The combined diethyl ether extracts were dried ($MgSO_4$), filtered and concentrated to a light-brown oil (0.63 g, 93%). The material was used without further purification.

Please replace paragraph [0145] with the following amended paragraph:

[0145] (1S,4S)-2-(5-(3-Thienyl)-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane

To a stirred solution of (1S,4S)-5-(5-(3-thienyl)-3-pyridyl)-2-(tert-butoxycarbonyl)-2,5-diazabicyclo[2.2.1]heptane (0.63 g, 1.4 mmol) in anisole (3.0 mL) at 0-5°C under a nitrogen atmosphere, trifluoroacetic acid (2.0 mL, 26 mmol) was added drop-wise over a 10 min period. After 0.5 h at 25°C, the solution was adjusted to pH 5 using 10% NaOH, followed by extraction

with diethyl ether (1 X 15 mL) to remove the anisole. The aqueous portion was adjusted to pH 11 using 10% NaOH, followed by extraction with diethyl ether (3 X 25 mL). The combined diethyl ether extracts were dried (Na_2SO_4), filtered and concentrated under vacuum. Purification of the residue by column chromatography on silica gel, using chloroform:methanol:triethylamine (40:5:1) as eluent, gave a light yellow oil (124 mg, 34%).

Please replace paragraph [0151] with the following amended paragraph:

[0151] In a sealed pressure tube under a nitrogen atmosphere, 3-benzoyl-5-bromopyridine (0.542 g, 2.1 mmol), (1S,4S)-N-(tert-butoxycarb- onyl)-2,5-diazabicyclo[2.2.1]heptane (0.475 g, 2.4 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.04 g, 0.04 mmol), ~~rac-2,2□-bis(diphenylphosphino)-1,1□-binaphthyl~~ rac-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.05 g, 0.08 mmol), sodium tert-butoxide (0.380 g, 3.8 mmol) and anhydrous toluene (20 mL) were stirred at 90°C for 20 h. The reaction mixture was cooled to room temperature and diluted with water (200 mL) and then extracted with diethyl ether (100 mL). The diethyl ether extract was dried ($MgSO_4$), filtered and concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel, using a gradient of 50% to 80% ethyl acetate:hexane as eluent, to yield 0.364 g (48%) of a yellow oil.

Please replace the Abstract with the following amended Abstract:

The present invention relates to diazabicyclic compounds, preferably to N-aryl diazabicyclic compounds. Of particular interest are 2-pyridinyl diazabicyclic compounds, such as (1S,4S)-2-(5-(3-methoxyphenoxy)-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane. Other exemplary compounds of the present invention include (1S,4S)-2-(5-(4-methoxyphenoxy)-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane, ~~(1S,4S)-2-(5-(3,4-dimethoxyphenoxy)-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane~~ (1S,4S)-2-(5-(3-thienyl)-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane, (1S,4S)-2-(5-(4-fluorophenoxy)-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane, and (1S,4S)-2-(5-benzoyl-3-pyridyl)-2,5-diazabicyclo[2.2.1]heptane. The present invention also relates to prodrug derivatives of the compounds of the present invention.